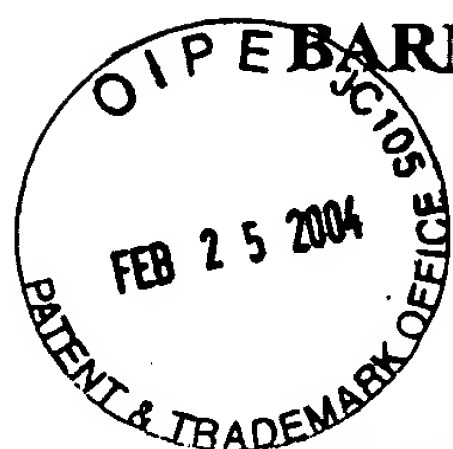


Serial No: 09/533,466

-1-

Attorney Docket No. 21416/90042



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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Group: 1631

Confirmation No.:

Application No.: 09/533,466

Invention: USE OF CRYSTAL STRUCTURE OF  
BACTERIAL IMP  
DEHYDROGENASE TO DESIGN  
INHIBITORS OF BACTERIAL  
GROWTH  
(New Title: CRYSTALS,  
MOLECULAR COMPLEXES, AND  
METHODS OF DEVELOPING LEAD  
COMPOUNDS FOR INHIBITORS OF  
BACTERIAL IMPDH)

Applicant: Frank Collart *et al.*

Filed: March 23, 2000

Attorney

Docket: 21416/90042

Examiner: A. Marschel

Certificate Under 37 CFR 1.8(a)

I hereby certify that this correspondence is being  
deposited with the United States Postal Service as  
Express Mail No. EL 990038911 US and addressed to  
the Commissioner for Patents, P.O. Box 1450  
Alexandria, VA 22313-1450

on February 25, 2004

(Signature)

Alice O. Martin

(Printed Name)

DECLARATION UNDER CFR 1.132

Assistant Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450  
Dear Sir:

1. I, Dr. Frank Collart, am a co-inventor of the patent application above.
2. I have read the Office Action mailed November 5, 2003 and I participated in the telephonic interview with Primary Examiner Marschel, Ph.D, on January 15, 2004.

Serial No: 09/533,466

-2-

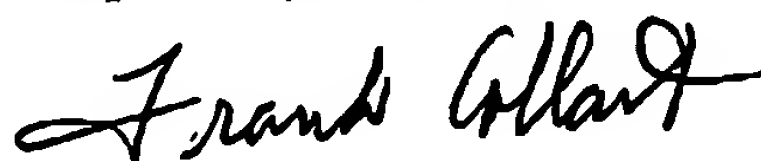
Attorney Docket No. 21416/90042

3. In response to what I understand is the examiner's question about the reproducibility of IMPDH crystal formation, I declare that I have successfully reproduced a IMPDH crystal at least four times by following the steps in the patent application on pages 18-19, and using *S. pyogenes* as also disclosed.

4. To demonstrate the uses of the reproduced crystal, complexes of purified IMPDH from *S. pyogenes* with IMP and four inhibitor molecules supplied by Pharmasset Inc. were prepared as described in the specification. Diffraction quality crystals were obtained for *S. pyogenes* IMPDH with IMP and each of the four Pharmasset NAD analogues (resolution range 2.1-2.3 Å). The high-resolution data provided a model for the complete structure of the bacterial enzyme and allowed comparison with the human IMPDH structure to identify differences that could be exploited in the design of specific inhibitors.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,



Frank R. Collart, Ph.D.

Dated: February 25, 2004